Ensuring a Robust U.S. Vaccine Industry: An FDA Perspective

Karen Midthun, M.D.
Deputy Director for Medicine
Center for Biologics Evaluation and Research
Philadelphia, BIO2005
June 20, 2005

CBER: Innovative Technology Advancing Public Health

- Protect and improve public and individual health in the US and, where feasible, globally
- Facilitate development, approval and access to safe and effective products and promising new technologies

What is FDA's role in regulating vaccines?

- Provides oversight and facilitates development of new vaccines under IND
- Licenses new vaccines based on demonstration of safety, efficacy, and quality of manufacture; continues to monitor product safety and manufacturing facilities after licensure
- Assists manufacturers in their efforts to maintain adequate availability of vaccines (e.g., expeditious review & interactions)

Streamlining the Regulatory Process: NVAC Recommendations (2003)

- Harmonizing content and format of regulatory submissions
- Review the implementation of cGMP standards
- Early and frequent communication between FDA and sponsors
- Review of regulatory process, including fast track, priority review, accelerated approval

International Harmonization Efforts

- International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals (ICH)
  - Has provided common guidance and format (Common Technical Document) for manufacturers pursuing approval in U.S., Europe, and Japan
  - Vaccines not addressed in some aspects of ICH
  - CBER follows ICH guidance relevant to vaccines and accepts the CTD format for vaccines

International Harmonization Efforts (cont.)

- CBER is a WHO collaborating center and participates in
  - Expert Committee for Biological Standards
  - Strategic Advisory Group of Experts
  - Global Advisory Committee on Vaccine Safety
  - Provides significant input on development of WHO guidelines for vaccines

International Harmonization Efforts (cont.)

- Confidentiality and information sharing agreements completed or being developed with regulatory counterparts (e.g., EMEA, Health Canada, MHRA, TGA, etc.)
  - Applicable to pre- and post-licensure issues
  - Enhance risk assessment/management and resource allocation
  - Encourage regulatory cooperation and prospective harmonization

International Harmonization Efforts (cont.)

- FDA is seeking membership in the Pharmaceutical Inspection Cooperation Scheme (PIC/S)
- PIC/S is a cooperative arrangement among international health authorities
- Purpose of PIC/S includes the international development, implementation, and maintenance of harmonized cGMP standards and quality systems of worldwide pharmaceutical inspectorates

Review of cGMP Standards

- FDA initiative on "Pharmaceutical cGMPs for the 21st Century"
  - To enhance and modernize regulation of pharmaceutical manufacturing and product quality
  - Launched August 2002
  - Final report issued September 2004 (www.fda.gov/cder/gmp/gmp2004/GMP_finalreport2004.htm)

"Pharmaceutical cGMPs for the 21st Century"

- Assessed existing cGMP programs
- Created new framework for regulatory oversight of manufacturing quality
  - Science and risk-based approach to review and regulation
  - Quality systems orientation
  - International cooperation
  - Strong public health protection
- Implementation underway, led by Council on Pharmaceutical Quality

Team Biologics Program

- Team Biologics evaluation and initiatives predate the cGMP initiative, but efforts are complementary
- Team Bio initiatives include development of systems-based compliance program for inspection of biological drug manufacturing facilities, including vaccines
  - Implemented December 1, 2004
  - Streamlined approach with levels based on compliance history

Team Biologics Program

- Team biologics quality system
  - CBER and ORA actively involved in establishing system of checks and balances (QC/QA)
  - Metrics developed for many processes and in implementation phase
- Additional training for investigators and product specialists conducted last fall.

Approaches to Facilitate Product Development and Licensure

- Early and frequent consultation between sponsor and FDA
- Fast track
- Priority review
- Continuing Marketing Applications: Pilots 1 and 2
- Accelerated approval
- Careful attention to risk/benefit and risk management issues

Early and Frequent Consultation

- Improves communication process
- Improves quality and efficiency of product development
- Reduces misunderstandings and potential for multiple review cycles
- CBER encourages pre-IND, end-of-phase 2, and pre-BLA meeting, and other communications that might be needed

Fast Track

- To facilitate development and expedite review of new drugs that are intended to treat serious or life-threatening conditions and that demonstrate potential to address unmet medical need
- Fast track designation applies to development program for specific indication, is granted during IND phase
- Provides for more frequent communications with the FDA (e.g., end-of-phase 1 meeting)
- May allow for a “rolling” submission of the BLA

Priority Review

- Product eligible if provides significant improvement in safety or effectiveness of treatment, diagnosis, or prevention of serious or life-threatening disease (CBER)
- Complete review of BLA in 6 months
- Review clock begins when the complete BLA has been submitted
- The pneumococcal conjugate vaccine, Prevnar, is an example of a vaccine that was given a priority review

Accelerated Approval

- Product eligible if provides meaningful therapeutic benefit over existing treatments for serious or life-threatening conditions
- Efficacy based on surrogate endpoint reasonably likely to predict clinical benefit
- Confirmatory post-marketing studies to verify clinical benefit
- Applicable to influenza vaccine, given vaccine supply below the ~185 million for whom CDC recommends vaccination

Continuous Marketing Application

- FDA conducting 2 pilots to determine if early review and additional feedback and advice to sponsors during drug development for selected products can further shorten drug development and review times
  - Pilot 1: FDA has agreed to provide discipline review letters under PDUFA timelines for pre-submitted reviewable units of a BLA (applies only to Fast Track designated products)
  - Pilot 2: frequent scientific feedback and interactions during drug development

Summary

- Despite ongoing challenges and increased responsibilities (e.g., counterterrorism activities, pandemic influenza preparedness, influenza vaccine shortage, etc.), FDA/CBER has made significant progress in addressing the NVAC recommendations on the national vaccine supply

Summary (cont.)

- CBER has adapted to challenging circumstances through extraordinary efforts, including proactive measures w/ sister agencies, industry, and others
  - Meetings to encourage developing new products
  - Early and intensive interactions w/ sponsors
  - Collaboration and rapid turnaround on INDs, EUAs
  - Proactive trips to inspect facilities
  - Participation in multiple product development teams
  - Targeted research to facilitate product development
  - Expedited reviews of key product applications
  - Increased communication with international regulatory counterparts

Regulation: What is the value added?

- Need for consistent and objective protection of the public's safety and need for trust
- Public expects safe and effective products, especially vaccines given to well individuals
- Preserving confidence in medical products and in public health leadership is critical
  - When things go "wrong," few will remember the crisis

Conclusions

- Regulation should facilitate development of new products and new technologies
- Greatly enhanced by good communication, transparency, and timely decision-making
- Regulatory actions are based on existing scientific knowledge and data
- Fundamental challenge for all: identify gaps in knowledge, pathways to address gaps, and define criteria for acceptability

Thanks!

- We welcome your input and ideas...
- Contact information:

Karen Midthun, M.D.

– Email: midthun@cber.fda.gov

– Phone number: 301 827 0372

CBER's Office of Communications, Training, and Manufacturers Assistance

– Phone number: 301 827 2000

– www.fda.gov/cber/manufacturer.htm